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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,579	12/06/2005	Hitoshi Niwa	0020-5374PUS1	4814

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BIRCH STEWART KOLASCH & BIRCH  
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FALLS CHURCH, VA 22040-0747

EXAMINER
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CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
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1632

NOTIFICATION DATE	DELIVERY MODE
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11/25/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/532,579	<b>Applicant(s)</b> NIWA ET AL.	
	<b>Examiner</b> Deborah Crouch, Ph.D.	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 11-26 and 30-40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-26 and 30-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 April 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/25/05, 1/25/07, 8/10/07, 11/8/07, 11/27/07</u> .            | 6) <input type="checkbox"/> Other: _____                          |



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Applicant's election without traverse of group II, claims 11-26 and 29 in the reply filed on March 11, 2008 is acknowledged. The amendment filed March 11, 2008 has been entered. Pending claims 11-26 and 30-40 are examined herein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-26 and 30-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

From a review of the specification and the art at the time of filing, claims 11-26 and 30-40 may be limited to a process for culturing mouse pluripotent stem cells comprising culturing mouse pluripotent stem cells in a medium comprising LIF, an antioxidant, and in the presence of an inhibitor of Adenylate cyclase activity or an *activator* of Adenylate cyclase activity. However, as the specification does not disclose the term *activator* of Adenylate cyclase activity, the limitation has on been given so as not to suggest new matter to applicant.

PACAP, BNP and ACTH, at the time of filing, and contrary to the specification, were recognized by the art to be *activators* of Adenylate cyclase (Gracia-Navarro, page 1069, col. 1, parag. 1, lines 1-3; Schorr, page 5806, col. 2, parag. 1, lines 4-7; and

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Yasuda, page 127-128, bridg. sent.. While applicant provides evidence that ACTH promotes mouse ES cell colony formation, ACTH functions as Adenylate cyclase activator does not change (specification, page 29, lines 6-19). The same analysis is true for BNP and PACAP. Further, the specification clearly teaches several art recognized Adenylate cyclase inhibitors to promote mouse ES cell colony formation (specification, page 31, lines 13-20). Therefore, the enablement rejection is due to the reliance in the claims on the medium supplement being "an inhibitor of Adenylate cyclase activity." Applicant may want to consider a non-mechanistic rendering of the claims if there is no support or evidence for ACTH, BNP and PACAP as such an inhibitor. From the evidence in the specification and that in the art at the time of filing, effect on Adenylate cyclase does not appear to be the causative action in inducing mouse ES cell growth under feeder free/serum free conditions.

At the time of filing, LIF was known in the art at the time of filing as an inhibitor of mouse ES cell differentiation when the mouse cells were grown in the absence of a feeder layer (Pera, page, col. 2, parag. 1, lines 7-9). In other words, LIF maintains pluripotency of mouse ES cells. According to the present disclosure, the invention relates to the growth of ES cells in the absence of feeder cells and serum (specification, page 27, lines 15-18). The maintenance of pluripotency is a requirement of applicant's method in parallel to ES cell growth or ES cell colony formation. Thus, it is required that the claimed method include an inhibitor of differentiation for the breath of "pluripotent stem cells." The only guidance provided in the specification for maintaining pluripotency is the culture in the presence of LIF (specification, page 29, lines 10-13). It is noted,

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however, that LIF does not maintain pluripotency in human ES, EC or EG cells (Pera, page, col. 2, parag. 1, lines 9-12). Thus, at the time of filing, for the claimed method to culture primate pluripotent stem cells, these cells would need to be cultured on feeder cells in addition to the Adenylate cyclase effectors claimed. The specification suggests these additives only induce pluripotent stem cell growth (specification, page 30, lines 16-18).

Thus, at the time of filing, the skilled artisan would have needed to engage in an undue amount of experimentation without a predictable degree of success to implement the invention for the breadth of the claims.

The claims are free of the prior art. At the time of filing, the prior art did not teach the culture of pluripotent stem cells under conditions that inhibit Adenylate cyclase activity. Pesce et al provides the closest prior art, but teaches PACAP is an Adenylate cyclase stimulator and promoter the growth of mouse PCG cells, which are not pluripotent cells. However, Pesce (Ref. CA) in combination with Shamlott et al. (1998) Proc. Natl. acad. Sci, Vol. 95, pp. 13726-13731. may be applied as an obviousness type rejection if the claims are amended to eliminate reference to Adenylate cyclase inhibitors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/  
Primary Examiner, Art Unit 1632

November 21, 2008